Remarks

After amendment, claims 1-16 remain pending in the present application, after canceling *without prejudice* claims 17-45 pursuant to the Examiner's restriction requirement and Applicant's decision to prosecute the invention of group I, namely claims 1-16. It is anticipated that Applicants will file a divisional application which is directed to subject matter which has been cancelled from this application. The amendment to the claims has been made to clarify the originally filed claims and to expedite allowance of the instant application. An active step (e) has been added to claim 1. Claim 13 has been amended to actively recite method steps from claim 1, which was referenced in originally filed claim 13, for purposes of clarity. No new matter has been added by way of this amendment.

The Examiner has rejected claims 1-16 variously under 35 U.S.C. §112, second paragraph and §102(b). For the reasons which are set forth in detail herein, including the enclosed paper from *Glycobiology* (Advance Access, July 31, 2006), which shows that the glycosylated hCG variant measured in the instant invention, ITA, is distinguishable from the N-linked glycosylated hCG variant measured by Kobota. This evidence clearly obviates the Examiner's rejection of the instant claims as being anticipated by Kobota. It is respectfully submitted that the instant claims are patentable over the disclosed prior art.

<u>The Rejection of Claims 1-16 under 35 U.S.C. §112, Second Paragraph</u>

The Examiner rejected original claims 1-16 under 35 U.S.C. §112, second paragraph as being incomplete for missing the step of determining the **total** amount of hCG in step 1b. In order to obviate the Examiner's rejection, claim 1 has been amended to reflect the fact that the total amount of hCG is measured in step b of claim 1. It is respectfully submitted that the claims are now in conformity with the requirements of 35 U.S.C. §112, second paragraph.

The Rejection of Claims 1-8 and 10-15 as Being Anticipated by Kobata

The Examiner has rejected claims 1-8 and 10-15 under 35 U.S.C. §102(b) as being anticipated by Kobata, *Biochemie,* 1988, 70: 1575-1585 ("Kobata"). It is the Examiner's contention that Kobata teaches a method of measuring ITA in a urine sample and on the basis of the percentage of ITA compared to the total amount of hCG in the sample, detecting invasive trophoblast cells if the percentage of ITA in the sample is greater than 30% of the total amount hCG. Applicant respectfully traverses the Examiner's rejection.

Essentially Applicant's method is clearly patentable and *not* anticipated by the method of Kobata simply because Kobata teaches measuring a variant of hCG which is not ITA, as that term has been defined in the specification. In particular, Kobata is directed to measuring N-linked glycosylated variant of hCG, not O-linked glycosylated variant hCG as in the present invention. Inasmuch as there are a number of glycosylated variants, it is the type of variant which will determine the accuracy of the assay and whether or not invasive trophoblast cells exist in a sample. In the case of Kobata, Kobata is measuring N-linked glycosylation of hCG, which is much less reliable than the measurement of O-linked glycosylation of hCG or ITA. Note that the definition of ITA, the O-linked glycolsylated variant which is measured in the present invention, is set forth in the specification at page 5, in the second full paragraph. This is the variant which Applicant has focused on and to which the present invention is directed to measuring. This is not what Kobata is measuring.

In contrast to the present method, Kobata *only* deals with and measures N-linked glycosylated hCG, not the O-linked glycosylated hCG which is measured in the present invention. Thus, the present invention clearly distinguishes over Kobata in measuring a different hCG variant than Kobata. Thus, because Kobata is not directed to the same or identical method as the present invention (because of the clearly distinguishable variants which are measured in the disclosure of Kobata vs. the present method), Kobata does not and cannot anticipate the present invention.

As further evidence for the distinction between the disclosure of Kobata and the instant method, Applicant encloses the paper Valmu, et al., "Site-specific glycan analysis of human chorionic gonadotropin β-subunit from malignancies and pregnancy by liquid chromatography-electrospray mass spectrometry, *Glycobiology Advance Access,* July 31, 2006. This paper clearly shows that the O-linked glycosylated hCG variant ITA, which is measured in the present method, is distinguishable over the N-linked glycosylated hCG which is measured by Kobata. Not only does the enclosed paper show the distinction between the N-linked and O-linked glycosylated variants of hCG, but also points to the superiority of measuring ITA- which is the only significant and consistent change in choriocarcinoma. Thus, Kobata, clearly is directed to measuring a different hCG variant and the disclosed method clearly does not anticipate the present invention.

The Rejection of Claims 1-5, 10 and 11 Being Anticipated by Cole, et al.

The Examiner has rejected originally filed claims 1-5, 10 and 11 under 35 U.S.C. §101(b) as being anticipated by Cole, et al., *Prenatal Diagnosis*, 1999, 19:351-359 ("Cole, et al") for the reasons which are set forth in the office action on pages 4-5. Essentially, the Examiner contends that originally filed claims 1-5, 10 and 11 are inherently anticipated by Cole, et al.

It is respectfully submitted that the presently pending claims, which set forth additional steps from the originally filed claims are clearly not anticipated by Cole, et al. The present method is directed to a method of determining that invasive trophoblast cells are present in a sample, a method which includes the step of making that determination based upon the relative percentage of ITA in the sample compared to total hCG in the sample. Cole, et al. is directed to a urinary screening test for fetal down syndrome- the publication does not even obliquely mention measuring ITA for determining the presence of invasive trophoblast cells. Moreover, regardless of whether the first four steps of claim 1 are inherently met by Cole, et al., certainly step e is not practiced by Cole, et al., nor is there even an oblique mention of such a determination or diagnosis step. Because

there are additional steps in the method of the present invention which are clearly not practiced by Cole, et al., the presently claimed invention is patentable over Cole, et al. It is respectfully submitted that the presently claimed invention is patentable over the art citred against the instant invention.

For the above reasons, Applicant respectfully asserts that the claims set forth in the amendment to the application of the present invention are now in compliance with 35 U.S.C. Applicants respectfully submit that the present application is now in condition for allowance and such action is earnestly solicited.

Applicants have not added any claim and have cancelled 29 claims (5 independent). No fee is therefore due for the presentation of this amendment. A petition for a two month extension of time is enclosed as is the fee for the extension. If any fee is due or any overpayment has been made, please charge/credit Deposit Account No. 04-0838. Should the Examiner wish to discuss the present application in an effort to advance its prosecution, the undersigned attorney may be reached at the telephone number set forth hereinbelow.

Respectfully submitted,

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By: _____
Henry D. Coleman
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Dated: October 30, 2006
Enclosure

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Certificate of Mailing

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as first class mail in an envelope addressed to: "Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450" on October 30, 2006.

_____
Henry D. Coleman (Reg. No. 32,559)